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Life, death, and the bridges in-between

Sam D. Shemie[1,2,3,4]

[1]Division of Critical Care and Extracorporeal Life Support Program, Montreal Children's Hospital, McGill University Health Centre, Montreal, Quebec, Canada. [2]Department of Pediatrics, McGill University, Montreal, Quebec, Canada. [3]The Bertram Loeb Chair in Organ and Tissue Donation, Faculty of Arts, University of Ottawa, Ottawa, Ontario, Canada. [4]Deceased Donation, Canadian Blood Services, Ottawa, Ontario, Canada

Address for correspondence: Sam D. Shemie, The Montreal Children's Hospital, 2300 Tupper Street, Room c-806, Montreal, Quebec, Canada H3H 1P3. sam.shemie@mcgill.ca

Remarkable advances in the technological capacity of modern medicine now permit the use of mechanical organ failure support deployed primarily to save life. Such technology serves as a bridge to either recovery or, when feasible, organ transplantation. However, when effective treatment options are exhausted, technological advances can be burdensome bridges to death. This paper briefly reviews the principles of management of life-threatening critical illness and the corresponding biological aspects of life, death, and organ donation, which are both informed and complicated by these technological and scientific achievements.

Keywords: end-of-life care; organ donation; transplantation; death; determination of death; life-sustaining treatments; withdrawal of life support; ECMO

The recent "Rethinking Mortality" series at the New York Academy of Sciences explored the evolving frontiers of life and death, arising from the profound scientific advances in modern medicine.[1] The ability to prolong life or suspend death through technology and treatments raises complex societal challenges, with crossings and collisions of science, law, ethics, and religion. The angst of end-of-life care decisions revolving around these technologies and treatments—What should be offered? What should be started? and When should it be stopped?—challenges patients, families, and healthcare providers on a daily basis. These questions of *quantity* of life, *quality* of life, and *quality of life worth living* are not merely moral and philosophical questions, they are concrete and real questions at the bedside, where these difficult decisions are made, and in the boardroom, where our economic capacity to sustain healthcare service delivery is under question.

Over the last 50 years, the advances in medicine, biology, and technology have been remarkable and have helped us in two major ways: saving patients and a better understanding of the biology of life and death. The specialties that have led to improving our understanding include cardiopulmonary resuscitation and physiology; mechanical ventilation; cardiac surgery and cardiopulmonary bypass; ICU-based life support; extracorporeal support and extracorporeal membrane oxygenation (ECMO); cell biology; and organ donation, preservation, and transplantation. These advances have been truly astonishing in the collective effort to save lives. They have also informed, and complicated, how medicine and modern society understands what it means to be alive, dying, or dead.

In any discussion about death, the profound emotional, psychological, and spiritual impact that the loss of a loved one has on family and friends cannot be overstated. Discussions about death are deeply emotional and sensitive. There are diverse philosophical, religious, and cultural perspectives when it comes to defining death, and a lack of understanding and awareness, not just among the public,[2] but also among health professionals[3] as well. Despite these challenges and various dimensions, it is important to understand how dying remains, first and foremost, a biological process. Death is an event in this biological process.

It is within the intensive care unit (ICU), where these intersections and collisions are routinely and most acutely confronted. In the ICU, during the

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treatment of life-threatening illness, sustaining life is based on delivering oxygen and nutrients to cells—specifically, to the mitochondria of the cells. This process provides energy for metabolic processes required for life. Trillions of cells are grouped together and make up our organs and tissues—all distinct structures with very distinct functions. Vital organs have basic functions: the lungs provide oxygen to the blood, the heart is the pump that circulates the blood containing oxygen, the liver metabolizes, and the kidney filters. The role of acute care and ICU professionals is to treat organ failure by recognizing life-threatening conditions and to intervene with life-sustaining treatments to maintain the delivery of oxygen to prevent death.

Technologies that support vital organs can sustain life in order for *time* or *treatment* to reverse the life-threatening condition. These complex, arduous, and resource-intensive treatments are extraordinarily successful, with survival rates ranging from 95% to 98% in children and 80% to 90% in adults. These treatments are fundamentally directed to provide oxygen delivery to the body. Without oxygen delivery, cells and organs stop working.

The dying process, which can be interrupted by life-sustaining intervention, is sequential and predictable. In general, death occurs by one of three physiological mechanisms:[4] (1) primary respiratory illnesses/events cause breathing to stop, resulting in a fall in oxygen levels in the blood, which finally causes the heart to stop pumping; (2) primary heart disease such as a heart attack—the heart arrests and cannot pump; and (3) catastrophic brain injury—the brain stops working, the brain's control of breathing is lost, breathing stops, oxygen drops, and the heart stops beating.

Remarkable advancements in technologies and transplantation permit the interruption of this dying process by supporting or replacing failing organs, with the assumption that time and/or treatment (medical and/or surgical) will reverse the disease. Organs can now be supported by machines such as artificial hearts (ventricular assist devices), artificial kidneys (dialysis machines or blood filtration systems), and breathing machines that effectively push oxygen into the blood stream or artificial lungs that completely replace lung function. These treatments and technologies can be used inside the body or deployed outside the body. Examples of extracorporeal, or outside of the body, technologies include ECMO[5] for respiratory failure or cardiac arrest, and heart–lung bypass machines used for open heart surgery. It is an incredible achievement to provide access to these complex heart/lung/kidney machines that can pump, circulate, oxygenate, and filter blood. They can *completely* replace the total arrest of heart/lung/kidney function. If that is the case, then how does one die?

These technologies serve as so-called bridges.[6–8] If the underlying life-threatening organ failure can improve with time or treatment, these technologies are *bridges to recovery*. If the failing organ cannot recover, they may become *bridges to transplantation*, but only if an organ transplant becomes available in time. In many unfortunate cases, when recovery is not possible and transplant is not an option or is unavailable, these technologies effectively become onerous *bridges to death*. In this case, the technologies allow us to keep organs of the body working artificially, even when all effective treatment options are exhausted. Unfortunately, this is a circumstance many families find themselves in when a loved one has a nonrecoverable illness and, on the basis of expert opinions of the healthcare team, must choose whether it is time to stop life-sustaining treatment. In ICUs worldwide, a decision to withhold and withdraw life support is the most common event preceding death.[9] The goals of care change from life saving to comfort measures, or a form of acute palliative care. In many countries, including Canada and the United States, the decision can only be made with agreement by the family, consistent with the wishes and values of the patient.

The emergence of modern intensive care, in the face of advancing organ support and replacement technologies, has challenged our ability to identify the margins of human viability. For example, the reversibility of cardiac arrest is now purely related to the context in which it occurs, in relation to the availability and application of support systems such as prolonged CPR and ECMO to maintain oxygenated circulation.[10] Complete and irreversible arrest of the heart may no longer be death, as long as oxygenated circulation to the body can be provided mechanically. More importantly, it has fundamentally changed the prevailing historical understanding of the essential aspect of personhood from the heart to the brain. It has become brain function—not heart or circulatory function—that defines the critical margin between life and death.[11]

The brain is responsible for our ability to breathe independently. The mechanism to sustain life after catastrophic brain injury is based on replacing the ability to breathe with a mechanical ventilator. However, unlike all other organs, the vital and fundamental clinical functions of the brain, responsible for who we are, cannot be replaced or supported. The brain controls consciousness, awareness, sensation, movement, thinking, feeling, and acting, as well as brainstem reflexes. Interaction and conducting an exchange of information with our environment depends on brain function. The commercial exchange of information[12] may be as neurologically complex as a verbal response to a posed question or as rudimentary as the pupil of the eye constricting to light.

Most treatments for any life-threatening illness, in supporting or replacing failing organs, are dedicated to preserving or restoring brain function. Regardless of the severity of the brain injury or the degree of the coma, the body and the organs can be kept alive indefinitely by replacing breathing with a machine (one that provides oxygen to the blood in order to keep the heart beating) and attentive ICU care. There are many diseases that cause catastrophic brain injuries, such as stroke, trauma, oxygen deprivation, and brain hemorrhage. If there is any degree of residual brain function, no matter how minimal,[13] the patient is still alive, and decisions to start, stop, or continue life-sustaining treatments are made by the family, or based on advance care directives, reliant on the prognostic information and advice provided by the medical team.

The most extreme form of brain injury is brain death. It is better understood as *brain arrest*,[14] which is the complete and permanent cessation of all clinical functions of the brain. All clinical functions of the brain have been lost and they will never resume—no ability to breathe independently, no capacity for any consciousness, no awareness, no sensations (no sight, smell, hearing, taste, pain, or feeling), no thinking, no emotions, no acting, no brainstem reflexes, and no interaction/exchange of information with the environment. The person has died. Brain death remains fundamentally based on the seminal work from the Harvard Ad Hoc Committee.[15] Death that is correctly diagnosed by neurological criteria[16] is not reversible—there is no chance of recovery of brain function.[17]

Conceptually, this means that the person can be dead as a result of complete and irreversible cessation of all brain function. However, their organs, which remain inside their bodies, may be kept alive. The public's and nonspecialist health professionals' ongoing misconceptions[3] regarding the essential aspect of the brain in personhood is manifest by confusion arising from recent media cases of brain death in pregnancy.[18] After brain death it is possible to sustain organ function with mechanical breathing, infection control, hormone replacement, and diligent ICU care for long periods of time to allow for fetal development to mature birth.[19] Effectively, these pregnant but brain dead mothers serve as life support systems for the baby, similar to extracorporeal life support systems such as ECMO, until the fetus is viable. It does not change the medical and legal fact that the mother remains a dead person with an artificially sustained body to allow the baby to be delivered, after which organ support systems are terminated.

While the advances in modern intensive care and life support technologies have complicated the line between life and death, clarity has been demanded by the concurrent success of organ transplantation. Through organ donation, transplantation saves lives. The majority of life-saving and life-preserving organ transplants occur through a process known as deceased donation, whereby organs are removed after death has been determined. Patients must be declared dead prior to the removal of vital organs for the purposes of transplantation. This Dead Donor Rule has been the central ethical, moral, and legal requirement that has historically guided transplantation. Deceased organ donation can therefore occur when a person has been declared dead because either their heart beat (circulatory death) or brain function (brain death) has completely and permanently ceased. Calls to abandon the Dead Donor Rule[20] are related to the aforementioned ethical, philosophical, and scientific debates regarding the complexities of defining the moment of death. Proposals to redefine organ donation eligibility to a point before death may have some theoretical merit. However, they ignore the inaccuracies of predicting those who inevitably will die, and pose troubling clinical challenges and a risk of abuse. In a voluntary system of organ donation based on public trust, the

Dead Donor Rule remains an indispensable ethical protection for dying patients.[21]

Organ donation is a benevolent act at the worst time—the juxtaposition of an unavoidable death in a willing donor to a preventable death in a transplant recipient. This gift is predicated on the public trust of the healthcare system, based on the first and foremost priority to save the life of the ill and injured whenever possible. The goal of every ICU team is to save lives—saving life through bridges to recovery, bridges to transplantation, or when all effective treatments are exhausted, bridges to death and organ donation.

Conflicts of interest

Sam D. Shemie, MD, works in the Division of Critical Care, Montreal Children's Hospital, McGill University Health Centre, where he is the Medical Director of the Extracorporeal Life Support Program, and is a professor of pediatrics, McGill University; Loeb Chair and Research Consortium in Organ and Tissue Donation, Faculty of Arts, University of Ottawa, and Medical Advisor, Donation, Canadian Blood Services. The views expressed are those of the author alone and do not necessarily represent the decisions, policy, or views of the Montreal Children's Hospital, McGill University, University of Ottawa, or Canadian Blood Services.

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